| Slaxo's Position Teva's Position | evidence quoted and cited in the discussion of claim 1 above. In addition, Glaxo wishes to call the Court's attention to the following intrinsic evidence | to claim 2. (Ex. 1): | 12. A pharmaceutical composition according to claim 11 wherein said pH is obtained by the use of | "The amount of ethanol present in the formulation is such that the resulting formulation has the <i>enhanced</i> | stability. Preferably the amount of ethanol in the composition on a weight/volume basis of the | complete formulation, is within the range 2.5% to "The amount of ethanol in the formulation for oral | more especially 7-8% w/v." (Emphasis added). complete formulation on a weight/volume basis, is | | "The amount of ethanol in the formulation for oral 8% ." | administration, expressed as a percentage of the complete formulation on a weight/volume basis, is | preferably within the range 2.5 to 10%, and more | particularly between 5 to 10%, more especially 7-8%." (Emphasis added). | $\Lambda/M_0/0$ | Ranitidine hydrochloride 1.68 | Ethanol 7.5 | Potassium dihydrogen | orthophosphate 0.095 | en orthophosphate |
|----------------------------------|---|---------------------------|--|--|--|--|--|-----------------------------------|---|--|--|---|-----------------|-------------------------------|-------------|----------------------|----------------------|---|
| | evidence quoted and ci 1 above. In addition, C Court's attention to the | specifically related to c | ,249 patent, Col. 1:54 | "The amount of ethanc such that the resulting | stability. Preferably th composition on a weig | complete formulation, | more especially 7-8% | 249 patent, Col. 2:30-34 (Ex. 1): | "The amount of ethano | administration, express complete formulation of | preferably within the ra | particularly between 5 7-8%." (Emphasis add | | | | | | *************************************** |

Glaxo's and Teva's Joint Claim Construction Chart for U.S. Patent No. 5,068,249

| Position | ds | qs qs 100ml." | | | | | | | | | | | | | | | A THE STATE OF THE |
|------------------|------------------------------------|--|--|--------|----------------------------------|----------------------|----------------|--|------------------------------|--------------|-------------------|---------|----------------------|-------------------|---|--|--|
| Teva's Position | Preservative | Sweetening agents Flavour Purified water BP to | | | | | | | | | | | | | | | ALA ALAMAHAYANINIANAYANINININANAYANINININANAYANINININANAYANINANA |
| ition | • []• | ormulation according | ation (150 mg/10 ml) ee base | 0/ M/V | 1.68 7.5 | | 0.095 | phate 0.350 | | | sb | ds | 100ml. | | nistory, Request for lated May 10, 1991 (Ex. 3, | Declaration of rovides convincing of the present cted advantage over 0 in terms of the composition. In this | liquid formulation |
| Glaxo's Position | '249 patent, Col. 2:47-65 (Ex. 1): | "An illustrative example of a formulation according to the invention is as follows | Ranitidine oral liquid formulation (150 mg/10 ml) expressed as free base | | Ranitidine hydrochloride Ethanol | Potassium dihydrogen | orthophosphate | Disodium hydrogen orthophosphate anhydrous | Hydroxypropylmethylcellulose | Preservative | Sweetening agents | Flavour | Purified water BP to | (Emphasis added). | '249 prosecution history, Request for Reconsideration dated May 10, 1991 G000202-11): | "Applicant submits herewith a Declaration of Dr. John Hempenstall which provides convincing evidence that the compositions of the present invention show a quite unexpected advantage over the teachings of GB-A-2142820 in terms of the stability of the ranitidine in the composition. In this | connection, it is noted that the liquid formulation |
| Claim Element | | | | | | | | | | | | | | | | | the special control of |

| Claim Element | Glaxo's Position Teva's Position |
|--|--|
| | without ethanol which is used in the Declaration for |
| | purposes of comparison is the same as the |
| | formulation of Example 3 of Padfield et al. |
| | Accordingly, the Declaration presents a direct |
| | present invention and a composition according to the |
| | prior art Applicant acknowledges that ethanol |
| | has previously been used in pharmaceutical |
| | compositions. However, the purpose for which |
| | ethanol has been included has been either as a solvent |
| | or as a preservative against bacterial contamination. There was however no reason to sumace that either |
| | of these functions of ethanol would have had any |
| | beneficial effects in terms of <i>limiting the degradation</i> |
| | of ranitidine in aqueous formulations thereof." |
| | (5/10/91 Request for Reconsideration, Ex. 3, |
| | G000205) (emphasis added). |
| | '249 prosecution history, Declaration of Dr. John |
| | Hempenstall executed April 12, 1991 (Ex. 3, G000208-11): |
| | "5. In my laboratory it was found that for an aqueous |
| | based ranifidine formulation, a significant and |
| | is achieved by the addition of ethanol to the |
| | formulation. |
| | * |
| | 6 The acceptable shelf life for an aqueous formulation containing ranitidine hydrochloride is |
| The state of the s | |

| Teva's Position | | | | | | |
|------------------|---|--------------------------------------|---|---|---|---|
| Glaxo's Position | considered to be the time at which no more than 5% of the ranitidine present in the formulation has degraded. Accordingly, the figure determined from the stability studies was the time (in months) for 5% ranitidine loss calculated as the lower 95% confidence limit. The results are as follows: | Without With 7.5% Ethanol Ethanol | Batch Batch Batch Batch Batch Temperature 1 2 3 4 5 | 30°C 12.5 13.6 19.5 17.0 20.8 37°C 5.4 4.7 7.8 7.1 7.5 45°C 1.8 2.3 2.9 2.9 2.8 | Thus, the formulation with ethanol has an average shelf life at 30°C of 19 months compared with 13 months when ethanol is excluded from the formulation. This is a highly significant and valuable improvement. | The stability of oral liquid formulations as described above except containing varying amounts of ethanol was also studied at 37°C and 45°C. The clear advantageous effects of the presence of ethanol can be seen from the following table which gives the time (in months) for 5% ranitidine loss (calculated as the lower 95% confidence limit). |
| Claim Element | | | | | | |

| Teva's Position | | | | Teva's Proposed Construction: 7% to 8% weight/volume ethanol. | Intrinsic Evidence: | '249 patent, claim 2 (Ex. 1): | "2. A pharmaceutical composition according to claim | based on the complete formulation." |
|-------------------|--|--|--|---|---|-------------------------------|---|---|
| Glaxo's Position. | Temperature % Ethanol 0 2.5 5.0 7.5 10.0 37°C 5.9 7.2 7.6 7.7 6.4 45°C 2.1 2.4 2.4 2.6 2.7 | 7. The above results clearly show that ethanol has a beneficial effect upon the stability of ranitidine in aqueous based formulations and furthermore I am not aware of any teaching in the art that would lead me to expect such an effect." (5/10/91 Request for Reconsideration, Ex. 3, ¶ 5, 6, 7 at G000209-211) (emphasis added). | | Glaxo's Proposed Construction: 7% to 8% weight/volume ethanol sufficient to enhance the | stability of the rainfudine active ingredient in the aqueous formulation for oral administration. | Intrinsic Evidence: | '249 patent, claim 1 (Ex. 1): | "A pharmaceutical composition which is an aqueous formulation for oral administration of an effective amount of ranitidine and/or one or more |
| Claim Element | | | Claims 3 (dependent on Claim 1) and 11 | "7% to 8% weight/volume | Cilianol | | | |

| Claim Element | Glaxo's Position | Teva's Position |
|--|--|--|
| | physiological acceptable salts thereof, said | '249 patent, claim 3 (Ex. 1): |
| | formulation comprising a stabilizing effective amount | |
| | of ethanol and said composition having a pH in the | "3. A pharmaceutical composition according to claim |
| | range of 6.5 to 7.5." (Emphasis added). | 1 containing 7% to 8% weight/volume ethanol based |
| | | on the complete formulation." |
| | '249 patent, claim 3 (Ex. 1): | 1940 matout alabar 11 (E. 1). |
| | WA whoman and in a common is in a common with the same | 243 patent, ciaim 11 (EA. 1). |
| | A pharmaceutical composition according to claim 1 | |
| | containing /% to 8% weight/volume ethanol based on the complete formulation." (Emphasis added). | 11. A pharmaceutical composition which is an |
| | | aduction containing 150 margaritation par 10 |
| | '249 patent, claim 11 (Ex. 1): | mill dose expressed as free base, said formulation |
| | and a framework for the section with the section of | having a pH in the range 7.0 to 7.3 and also |
| | formulation of somitiding for and observation | containing 7% to 8% weight/volume ethanol based |
| | containing 150 mg ranitidine per 10 ml dose | on the complete formulation. |
| | | |
| | pH in the range of 7.0 to 7.3 and also containing 7% | '249 patent, claim 12 (Ex. 1): |
| | to 8% weight/volume ethanol based on the complete | 12 A pharmacentical composition according to |
| | formulation." (Emphasis added). | claim 11 wherein said pH is obtained by the use of |
| | Glaxo incomorates by reference all of the intrinsic | buffer salts. |
| | evidence cited and quoted in the discussion of claims | |
| | 1 and 2. In addition, Glaxo wishes to call the Court's | '249 patent, Col. 2:30-34 (Ex. 1): |
| | attention to the following intrinsic evidence | |
| | specifically related to claims 3 and 11. | "The amount of ethanol in the formulation for oral |
| | | administration, expressed as a percentage of the |
| | '249 patent, Col. 1:54-56 (Ex. 1): | complete formulation on a weight/volume basis, is |
| | | preferably within the range 2.5 to 10%, and more |
| | "The amount of ethanol present in the formulation is | particularly between 5 to 10%, more especially 7- |
| | such that the resulting formulation has the <i>enhanced</i> | 8%." |
| PARTICIPATION OF THE PARTICIPA | stability. Preferably the amount of ethanol in the | ALTHOUGH AND THE CONTRACTOR OF THE PROPERTY OF |

| Claim Element | Glaxo's Position | Teva's Position | |
|--|--|------------------------------------|---|
| | composition on a weight/volume basis of the complete formulation, is within the range 2.5% to | '249 patent, Col. 2:53-65 (Ex. 1): | |
| | 10%, and more particularly is between 5 to 10% w/v, more especially 7-8% w/v." (Emphasis added). | "Ranitidine or | 0ml) |
| | '249 patent, Col. 2:47-65 (Ex. 1): | expressed as free base | |
| | ."An illustrative example of a formulation according | 1 | *************************************** |
| | to the invention is as follows | Potassium dihydrogen | |
| | Ranitidine oral liquid formulation (150 mg/10ml) | orthophosphate 0.095 | |
| | expressed as free base | anhydrous 0.350 | |
| | A/M % | ylmethylcellulose | |
| | ne hydrochloride | | *************************************** |
| | Ethanol 7.5 | Sweetening agents qs | |
| | Potassium dihydrogen | | |
| | orthophosphate 0.095 | Purified water BP to 100ml." | |
| | drogen orthophosphate | | |
| | anhydrous 0.350 | | |
| | Hydroxypropylmethylcellulose qs | | |
| | Preservative qs | | |
| | Sweetening agents qs | | |
| | • | | |
| | Purified water BP to 100ml. | 2 | |
| | (Emphasis added). | | |
| | '249 prosecution history, Request for Reconsideration dated May 10, 1991 (Ex. 3, G000202-11): | | |
| | "Applicant submits herewith a Declaration of Dr. John Hempenstall which provides convincing | | - |
| HITTINGS MATARITIS OF THE PARTICULAR PROPERTY OF THE PARTICULAR PROPERTY OF THE PROPERTY OF THE PARTICULAR PAR | The second secon | | |

| Teva's Position | | | | | | | | | | | | | | | | | | | | | | | | |
|------------------|---|--|---|---|--|---|--|---|--|---|--|--|--|--|--|---|---|---|---|--------------|---|---|---|--------------|
| Glaxo's Position | evidence that the compositions of the present | invention show a quite unexpected advantage over | the teachings of GB-A-2142820 in terms of the | stability of the rantitaine in the composition. In this connection, it is noted that the liquid formulation | without ethanol which is used in the Declaration for | purposes of comparison is the same as the | Accordingly, the Declaration presents a direct | comparison between a composition according to the | present invention and a composition according to the | prior art Applicant acknowledges that ethanol | has previously been used in pharmaceutical | compositions. However, the purpose for which | or as a preservative against bacterial contamination | There was, however, no reason to suppose that either | of these functions of ethanol would have had any | beneficial effects in terms of limiting the degradation | of ranitidine in aqueous formulations thereof." | (5/10/91 Request for Reconsideration, Ex. 3, G000205) (emphasis added). | 1249 prosecution history, Declaration of Dr. John | G000208-11): | "5. In my laboratory it was found that for an aqueous | based ranitidine formulation, a significant and | surprising enhancement in the stability of ranitidine is achieved by the addition of ethanol to the | formulation. |
| Claim Element | | | | | | VVVVIII 100 00 00 00 00 00 00 00 00 00 00 00 00 | | | | | | | | | | | | | | | | | | |

| Teva's Position | 9 1 | | P | | ole . | P |
|------------------|---------------------------------------|--------------------------------------|---|---|---|--|
| Glaxo's Position | * * * * * * * * * * * * * * * * * * * | Without With 7.5% Ethanol Ethanol | Batch Batch Batch Batch Batch Temperature 1 2 3 4 5 | 30°C 12.5 13.6 19.5 17.0 20.8 37°C 5.4 4.7 7.8 7.1 7.5 45°C 1.8 2.3 2.9 2.9 2.8 | Thus, the formulation with ethanol has an average shelf life at 30°C of 19 months compared with 13 months when ethanol is excluded from the formulation. This is a highly significant and valuable improvement. | The stability of oral liquid formulations as described above except containing varying amounts of ethanol was also studied at 37°C and 45°C. The clear advantageous effects of the presence of ethanol can |
| Claim Element | | | | | | |

| Teva's Position | | | Teva's Proposed Construction: This clause need not and should not be construed, given Teva's judicial admission, as stated during the June 30, 2005 telephone conference with the Court. |
|---|--|--|--|
| Glaxo's Position be seen from the following table which gives the time (in months) for 5% ranitidine loss (calculated as the lower 95% confidence limit) | Temperature % Ethanol 0 2.5 5.0 7.5 10.0 37°C 5.9 7.2 7.6 7.7 6.4 45°C 2.1 2.4 2.4 2.6 2.7 | 7. The above results clearly show that ethanol has a beneficial effect upon the stability of ranitidine in aqueous based formulations and furthermore I am not aware of any teaching in the art that would lead me to expect such an effect." (5/10/91 Request for Reconsideration, Ex. 3, ¶¶ 5, 6 and 7 at G000209-211) (emphasis added). | Glaxo's Proposed Construction: A water based formulation, wherein water is the solvent (i.e., the liquid present in the formulation in the largest amount), administered orally for gastrointestinal absorption. |
| Claim Element | | | Claims 1-10 "aqueous formulation for oral administration" |

| Teva's Position | | | | | | |
|--------------------------------------|------------------------------------|---|-----------------------------------|--|---------------------------|---|
| Glaxo's Position Intrinsic Evidence: | '249 patent, Col. 1:40-44 (Ex. 1): | "We have now surprisingly found that the stability of ranitidine in aqueous based formulations and more particularly aqueous based formulations for oral administration may be substantially enhanced by the addition of ethanol to the formulation." (Emphasis added). | '249 patent, Col. 2:1-10 (Ex. 1): | "A preferred embodiment of the invention is an aqueous formulation for oral administration. Such a formulation may comprise ranitidine and/or one or more of its physiologically acceptable salts dissolved in water, ethanol, a preservative and a viscosity enhancing agent. Preferably the required pH of the formulation is obtained by the use of appropriate buffer salts. Optionally the composition may also contain other conventional excipients such as a sweetener, a flavour and/or flavouring aids." (Emphasis added). | '249 patent, Col. 2:38-43 | "The aqueous formulations for oral administration are conveniently prepared by mixing an aqueous solution of ranitidine and/or one or more of its physiologically acceptable salts together with ethanol and the excipients, with aqueous solution or |
| Claim Element | | | | | | |

| Teva's Position | | | | | | | | | | | | | | | | | | | | | | |
|------------------|---|------------------------------------|--|---|---------------------------------|--------------------------|---------|----------------------|----------------|----------------------------------|-----------|------------------------------|--------------|-------------------|---------|----------------------|-------------------|---|--|---|---|--|
| | ing agent." | *** | nulation according | on (150 mg/10ml) oase | Λ/M ⁰ / ₀ | 1.68 | 7.5 | | 0.095 | | 0.350 | ds | ds | ds | ds | 100ml. | | ation of Dr. John | 1991 (Ex. 3, | that for an | tion, a significant | stability of ion of ethanol to |
| Glaxo's Position | dispersion of the viscosity enhancing agent." | '249 patent, Col. 2:47-65 (Ex. 1): | "An illustrative example of a formulation according to the invention is as follows | Ranitidine oral liquid formulation (150 mg/10ml) expressed as free base | | Ranitidine hydrochloride | Ethanol | Potassium dihydrogen | orthophosphate | Disodium hydrogen orthophosphate | anhydrous | Hydroxypropylmethylcellulose | Freservative | Sweetening agents | Flavour | Purified water BP to | (Emphasis added). | '249 prosecution history, Declaration of Dr. John | Hempenstall executed April 12, 1991 (Ex. 3, G000208-11): | "5. In my laboratory it was found that for an | aqueous based ranitidine formulation, a significant | ranitidine is achieved by the addition of ethanol to |
| Claim Element | | | | | | | | | | | | | | | | | | | | | | |

| Claim Element | Glaxo's Position | Teva*s Position |
|--|--|---|
| | the formulation. | |
| | * | |
| | 7. The above results clearly show that ethanol has a beneficial effect upon the stability of ranitidine in aqueous based formulations and furthermore I am | |
| | not aware of any teaching in the art that would lead me to expect such an effect." (5/10/91 Request for | |
| | Reconsideration, Ex. 3, | |
| A CONTRACTOR OF THE CONTRACTOR | | |
| Claims 11-12 | | |
| "aqueous formulation of ranitidine suitable | Glaxo's Proposed Construction: A water based formulation of ranitidine. wherein water is the | Teva's Proposed Construction: This clause need not and should not be construed, given Teva's judicial |
| for oral | solvent (i.e., the liquid present in the formulation in | admission, as stated during the June 30, 2005 |
| administration | the largest amount), administered orally for gastrointestinal absorption. | telephone conference with the Court. |
| | Intrinsic Evidence: | |
| | '249 patent, Col. 1:40-44 (Ex. 1): | |
| | "We have now surprisingly found that the stability of ranitidine in aqueous based formulations and more | |
| | particularly aqueous based formulations for oral administration may be substantially enhanced by the addition of ethanol to the formulation." (Emphasis | |

Glaxo's and Teva's Joint Claim Construction Chart for U.S. Patent No. 5,068,249

| Teva's Position | | | | | | | | | | | | |
|------------------|---------|---|---|---|---|---|---------------------------|--|--|---|-----------|--|
| Glaxo's Position | added). | " | A preferred embodiment of the invention is an aqueous formulation for oral administration. Such a formulation may comprise ranitidine and/or one or | inote of its physiologically acceptable saits <i>dissolved</i> in water, ethanol, a preservative and a viscosity enhancing agent. Preferably the required pH of the | formulation is obtained by the use of appropriate buffer salts. Optionally the composition may also | contain other conventional excipients such as a sweetener, a flavour and/or flavouring aids." (Emphasis added). | '249 patent, Col. 2:38-43 | "The aqueous formulations for oral administration are conveniently prepared by mixing an aqueous | solution of raintume analor one or more of its physiologically acceptable salts together with ethanol and the excipients, with aqueous solution or | dispersion of the viscosity enhancing agent." | | |
| Claim Element | | | | | | | | | | | manananan | |

Glaxo's and Teva's Joint Claim Construction Chart for U.S. Patent No. 5,068,249

| Teva's Position | | 50 | | | | | 6 G | | |
|------------------|------------------------------------|--|---|-------------------------------------|--|---|--|--|--|
| | | llation according | 1 (150 mg/10ml) | 1.68 | 0.095 | 0.350 qs qs | qs qs 100ml. | tion of Dr. Joh 991 (Ex. 3, | hat for <i>an</i> on, a significant stability of on of ethanol to |
| Glaxo's Position | '249 patent, Col. 2:47-65 (Ex. 1): | "An illustrative example of a formulation according to the invention is as follows | Ranitidine oral liquid formulation (150 mg/10ml) expressed as free base | Ranitidine hydrochloride Ethanol | Potassium dinydrogen orthophosphate Disodium hydrogen orthophosphate | anhydrous Hydroxypropylmethylcellulose Preservative | Sweetening agents Flavour Purified water BP to (Emphasis added). | '249 prosecution history, Declaration of Dr. John Hempenstall executed April 12, 1991 (Ex. 3, G000208-11): | "5. In my laboratory it was found that for an aqueous based ranitidine formulation, a significant and surprising enhancement in the stability of ranitidine is achieved by the addition of ethanol to the formulation. |
| Claim Element | | | | | | | | | |

Glaxo's and Teva's Joint Claim Construction Chart for U.S. Patent No. 5,068,249

| Teva's Position | |
|------------------|---|
| * | at ethanol has a ranitidine in hermore I am hat would lead 91 Request for G000209, 211) |
| Glaxo's Position | 7. The above results clearly show that ethanol has a beneficial effect upon the stability of ranitidine in aqueous based formulations and furthermore I am not aware of any teaching in the art that would lead me to expect such an effect." (5/10/91 Request for Reconsideration, Ex. 3, ¶ 5 and 7 at G000209, 211) (emphasis added). |
| * | 7. The above results beneficial effect upon aqueous based formu not aware of any teac me to expect such an Reconsideration, Ex. (emphasis added). |
| Claim Element | |

Dated: June 30, 2006

CONNOLLY BOVE LODGE & HUTZ LLP

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CERTIFICATE OF SERVICE

I hereby certify that on June 30 2006, I electronically filed the foregoing **JOINT CLAIM CONSTRUCTION CHART FOR U.S. PATENT NO. 5,068,249** with the Clerk of Court using CM/ECF which will send notification of such filing and we will hand deliver such filing to the following:

Josy W. Ingersoll, Esq. Young Conway Stargatt & Taylor The Brandywine Building 1000 West Street, 17th Floor P.O. Box 391 Wilmington, DE 19899

I hereby certify that on June 30, 2006, I have mailed via Federal Express, the document to the following non-registered participants:

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